



Complete Summary

GUIDELINE TITLE

UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure.

BIBLIOGRAPHIC SOURCE(S)

Fisher M, Benn P, Evans B, Pozniak A, Jones M, Maclean S, Davidson O, Summerside J, Hawkins D, Clinical Effectiveness Group (British Association for Sexual Health and HIV). UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure. Int J STD AIDS 2006 Feb;17(2):81-92. [84 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [September 10, 2007, Viracept \(nelfinavir mesylate\)](#): Pfizer issued a Dear Healthcare Professional Letter to inform healthcare professionals of the presence of ethyl methanesulfonate (EMS), a process-related impurity in Viracept and to provide guidance on the use of Viracept in pregnant women and pediatric patients.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

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SCOPE

DISEASE/CONDITION(S)

Human immunodeficiency virus (HIV) infection

GUIDELINE CATEGORY

Counseling
Evaluation
Management
Prevention
Risk Assessment

CLINICAL SPECIALTY

Allergy and Immunology
Emergency Medicine
Family Practice
Infectious Diseases
Internal Medicine
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Public Health Departments
Social Workers

GUIDELINE OBJECTIVE(S)

To ensure the appropriate use of post-exposure prophylaxis (PEP) following potential sexual exposure (PEPSE) to human immunodeficiency virus (HIV) as a potential method of preventing HIV infection

TARGET POPULATION

Patients at risk for human immunodeficiency virus (HIV) infection due to sexual exposure to HIV

INTERVENTIONS AND PRACTICES CONSIDERED

1. Risk assessment to determine whether post-exposure prophylaxis (PEP) following potential sexual exposure (PEPSE) is appropriate
2. PEPSE regimens implemented as soon as possible after the exposure

- Triple agent regimens that may use nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs).
 - Modification of PEP antiretroviral therapy in relation to drug history or resistance testing, if available, in patients with current or past history of treatment failure
3. Management of treatment side-effects
 4. HIV testing prior to and shortly after initiation of PEPSE and at three and six months
 5. Referral to a Health Advisor (or appropriately experienced health care worker)
 6. Regular medical follow-up and patient encouragement
 7. Comprehensive screening for other sexually transmitted diseases (STIs)
 8. Consideration of Hepatitis B vaccination (and immunoglobulin)
 9. Risk reduction counseling
 10. Counseling of repeat users of PEPSE

MAJOR OUTCOMES CONSIDERED

- Transmission of HIV infection
- HIV seroconversion
- Efficacy of post-exposure prophylaxis (PEP)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The development of this guideline included a writing group with representatives from British Association for Sexual Health and HIV (BASHH), British HIV Association (BHIVA), Expert Advisory Group on AIDS (EAGA), Society of Sexual Health Advisers (SSHA), Health Protection Agency (HPA), the HIV and Sexual Health Group of the British Psychological Association, the Terrence Higgins Trust (THT) and the National AIDS Trust (NAT). Patients' perspectives were considered by involvement of THT, NAT and discussion at a stakeholder group organized by THT and the Community HIV and AIDS Prevention Strategy (CHAPS) conference.

The guideline is based upon a comprehensive review of the literature pertaining to post-exposure prophylaxis (PEP) following potential sexual exposure (PEPSE). The recommendations are based upon a combination of biological plausibility, cohort studies, data from PEP in other settings, and expert opinion. The recommendations are the result of a series of meetings of the writing committee and the input from the consultation process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

There is no conclusive data regarding the cost effectiveness of post-exposure prophylaxis (PEP) following potential sexual exposure (PEPSE). It has been argued that the cost of providing PEP may be effectively spent on other prevention initiatives. However, while the drug cost of a full 28-day course of PEP is approximately 600 pounds sterling, the lifetime costs of treatment for an HIV positive individual are estimated to be between 135,000 and 181,000 pounds sterling. A retrospective cost analysis of the San Francisco PEPSE programme has shown it to be cost-effective when used in high-risk exposures and potentially cost saving when used after receptive anal intercourse in men who have sex with men (MSM). Subsequent modelling utilizing data from many United States cities suggests similar levels of cost-effectiveness providing PEPSE is targeted to high-risk exposures consistent with those recommended within these guidelines.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Prior to publication the final draft was placed on the British Association for Sexual Health and HIV (BASHH) website and copies circulated to the Terrence Higgins Trust (THT), the British HIV Association (BHIVA), and the Department of Health for comment and peer review. After a period of 12 months, any comments received were reviewed by the guideline authors, and acted upon appropriately, before final authorization by the Clinical Effectiveness Group (CEG) was given and publication was undertaken.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations for Prescribing Post-Exposure Prophylaxis (PEP) Following Potential Sexual Exposure (PEPSE)

It is crucial to consider PEPSE as only one strategy in preventing human immunodeficiency virus (HIV) infection and, as such, it should be considered as a last measure where conventional, and proven, methods of HIV prevention have failed.

A risk versus benefit analysis should be undertaken for every individual presenting following an exposure and the decision to initiate PEP made on a case-by-case basis. This should consider both the risk of transmission according to coital act (as in Table 2 in the original guideline document) and the risk of the source being HIV positive (as in the Table 1 in the original guideline document). Consideration should be given to the possibility of the presenting individual having already been infected with HIV, and the ability to adhere to and tolerate the proposed antiretroviral drug regimen. The potential exposure to other sexually transmitted infections (STIs) and appropriate management for this needs to be considered alongside consideration of provision of PEPSE. The wishes of the individual should be considered at all times.

Situations in which PEPSE Would Be Considered

The use of PEPSE following potential sexual exposure to HIV is only recommended where the individual presents within 72 hours of exposure. Within that time frame, it is recommended that PEPSE (if given) should be administered as early as possible. All recommendations are for either unprotected sexual exposure or where condom failure has occurred. Recommendations regarding fellatio are where the partner giving fellatio is presenting for PEPSE.

Source Individual Is Known to Be HIV Positive

Receptive anal sex	Recommended
Insertive anal sex	Recommended
Receptive vaginal sex	Recommended
Insertive vaginal sex	Recommended
Fellatio with ejaculation	Considered
Splash of semen into eye	Considered

Fellatio without ejaculation	Not recommended
Cunnilingus	Not recommended

Source Individual Is of Unknown Status

Attempt should be made, where possible, to establish the HIV status of the source individual (according to appropriate guidance on HIV testing and consent) as early as possible. There is growing evidence to suggest that significant cases of PEP can be averted through assertive HIV testing of the source individual. It is therefore recommended that strong efforts be made to encourage the individual to notify their partner where possible, and for the clinic to arrange urgent HIV testing of that partner, with appropriate guidance on HIV testing and consent, as early as possible.

Source Is from a Group or Area of High HIV Prevalence

Receptive anal sex	Recommended
Insertive anal sex	Considered
Receptive vaginal sex	Considered
Insertive vaginal sex	Considered
Fellatio with ejaculation	Considered

Source Is Not from a Group or Area of High HIV Prevalence

Receptive anal sex	Considered
Insertive anal sex	Not recommended
Receptive vaginal sex	Not recommended
Insertive vaginal sex	Not recommended
Fellatio with ejaculation	Not recommended

High prevalence groups within this recommendation are those where there is a significant likelihood of the source individual being HIV positive. Within the United Kingdom (UK) at present, this is likely to be men who have sex with men (MSM) and individuals who have immigrated to the UK from areas of high HIV prevalence (particularly sub-Saharan Africa).

Sexual assault: It is believed that transmission of HIV is likely to be increased following aggravated sexual intercourse (anal or vaginal), such as that experienced during sexual assault. Clinicians may therefore consider recommending PEPSE more readily in such situations. While the routine recommendation of PEPSE is likely to be appropriate in high prevalence situations, it is likely that the strength of recommendation and subsequent uptake will be lower in UK settings unless the 'donor' is perceived to be from a high-prevalence group.

Other factors which may alter the strength of recommendation: Where factors are present which are believed to influence the probability of HIV transmission - presence of concurrent sexually transmitted infection (STI), knowledge of viral load in the 'donor' - the strength of these recommendations may be increased or decreased appropriately.

Recommendations for Drug Regimens to Be Used

The choice of drugs to be used for PEP is drawn from those used in established infection. These include the nucleoside reverse transcriptase inhibitors (NRTIs), the non-nucleoside reverse transcriptase inhibitors (NNRTIs) and the protease inhibitors (PIs). In addition the nucleotide tenofovir has shown activity as PEP in an animal (simian immunodeficiency virus [SIV]/macaque) model of sexual exposure and is currently being evaluated in high-risk populations as monotherapy for pre-exposure prophylaxis. Other classes of drugs such as entry inhibitors (T20) will need to be considered as they become available for established infection. Zidovudine (an NRTI) is the only drug to date which has been studied and for which there is evidence of reduction of risk of HIV transmission following occupational exposure. It is for this reason that many consider it to be reasonable that zidovudine is included in all first choice PEP regimens, unless there is evidence that the source virus is resistant to this drug, or that there is significant intolerance. However, it is theoretically likely that alternative nucleosides will be equally effective. Some recent studies suggest that a tenofovir-containing regimen may be better tolerated than zidovudine; therefore, it would be reasonable to offer this as an alternative either at initial presentation or if zidovudine-related side-effects occur.

In established HIV infection, combination drug therapy with at least three drugs is more effective than monotherapy or dual drug regimens. It is thus recommended, when there is considered to be a significant risk of HIV transmission following risk assessment, that a triple agent regimen be advised. Theoretical considerations to support the recommendation of three drugs include the later presentation of patients for PEPSE and giving drugs with different resistance patterns as any resistant virus in the source may be unknown.

Nevirapine is not recommended due to the high rates of hepatotoxicity and potential for fulminant hepatic failure when used in this setting. Efavirenz has a lower incidence and severity of rash, but this reaction may still cause anxiety and diagnostic confusion. Furthermore efavirenz causes short-term psychostimulation, which is possibly less well tolerated in anxious patients receiving PEP than in patients with established HIV infection.

The routine use of abacavir is also not recommended. A hypersensitivity reaction is reported in up to 8% of patients with established infection. Although the risk has not been assessed in HIV negative individuals, it is recommended to reserve the use of abacavir for when first-line treatments are not thought appropriate.

It is recommended that the choice of antiretroviral regimen prescribed should follow consideration of local epidemiology of drug resistance, particularly the incidence of primary resistance which may be increasing in some parts of the UK.

Individuals who are already well informed regarding the safety, tolerability and efficacy profiles of individual antiretroviral agents may have their own individual perspective on which agents they would prefer to take. Such choices should, where possible, be respected but may be affected by the composition of 'starter packs', the possible resistance 'history' of the donor, local HIV primary resistance rates, and must involve consideration of toxicity profiles in the uninfected.

Recommended Combinations

2NRT1[#] + PI* (boosted PI⁺)

* - Nelfinavir

+ - Lopinavir or fosamprenavir or saquinavir

- (azidothymidine [AZT] & epivir [3TC]) or (stavudine [D4T] & 3TC) or (tenofovir & 3TC) or (tenofovir & emtricitabine [FTC])

Other triple combinations in use for established infection may also be considered reasonable choices and a number are currently being evaluated in international studies.

If there is evidence that the source patient has current or past history of treatment failure, the PEP antiretroviral therapy should be modified in relation to the drug history and/or to resistance testing if available. Expert advice should be sought.

Starter packs As with the guidelines for occupational exposure, it may be helpful to use a starter pack (3 to 5 days medication). Should PEP starter packs be used, suitable combinations would be Combivir® (zidovudine 300 mg plus lamivudine 150 mg) twice daily (bd) plus nelfinavir 1250 mg bd. An alternative to Combivir would be Truvada® (tenofovir 245 mg plus emtricitabine 200 mg). An alternative to nelfinavir would be a boosted PI such as lopinavir/ritonavir 3 capsules bd or fosamprenavir 700 mg bd with ritonavir 100 mg bd (or 1400 mg once daily [od] with ritonavir 200 mg od). The need for refrigeration of ritonavir and Kaletra® may inhibit their use as starter packs; an alternative strategy may be to switch to one of these agents after expert review.

This PEPSE regimen can be continued or modified at initial review within five days, depending on further information about the source virus and the patient's tolerance of the medication.

Side-effects Any of the antiretroviral drugs may have side effects, which appear to be less well tolerated in HIV-negative patients receiving PEP than HIV-positive individuals starting treatment. Many of these can be managed symptomatically, for example the use of anti-nauseants and antidiarrhoeals with the combination of Combivir and nelfinavir. Close monitoring and follow-up of individuals receiving PEPSE is recommended to manage such side effects and thereby optimize completion rates.

Duration of treatment The optimal duration of PEP is unknown. However, animal studies and a case-controlled study of health care workers suggest that four weeks is required to minimize the potential for HIV transmission. It is recommended therefore that four weeks of PEP should be utilized in the sexual exposure setting (unless source-testing after initiation of PEPSE determines that the 'donor' is HIV-negative).

Service Provision to Enable Appropriate Use of PEPSE

Given that, for optimal efficacy, PEPSE should be commenced as soon as possible after exposure, 24-hour access should be available. As with PEP following occupational exposure, it is recommended that local policies and pathways be established to enable this.

It is therefore likely that accident & emergency (A&E) departments will be expected to assume significant responsibility for provision of PEPSE, with the need for support and training from areas of local expertise. Such areas are likely to be Departments of Genitourinary (GU) Medicine, HIV Medicine, Infectious Diseases or Virology/Microbiology. The training issues are essentially those outlined comprehensively in the Department of Health/Expert Advisory Group (DH/EAGA) on acquired immunodeficiency syndrome (AIDS) guidance on HIV PEP.

It is recommended that individuals presenting for PEPSE should be referred and seen as early as possible by a clinician experienced in the management of antiretroviral therapy and with expertise in HIV testing and transmission - whether or not PEPSE is offered or accepted. PEPSE should not be withheld until such expertise is available. However, it is recommended that local policies should include 24-hour access to advice from an experienced HIV clinician, particularly for cases where the PEPSE regimen may need to be adjusted to reflect possible drug resistance in the 'donor'.

Assessment and Initial Management of the Individual Presenting for PEPSE

It is essential that an appropriate risk assessment is performed to enable provision of PEPSE according to the recommendations outlined above.

At presentation, and prior to administration of PEPSE, the following issues must be discussed with the individual:

- The rationale for PEPSE
- The lack of conclusive data for the efficacy of PEPSE
- The potential risks and side effects of PEPSE
- The arrangement for early follow-up with an HIV/genitourinary medicine (GUM) clinician

The use of a consent form is not considered essential, but documentation must demonstrate that these issues have been discussed.

It is mandatory that individuals for whom PEPSE is provided to undertake an HIV test (with rapid result) prior to, or shortly after initiating therapy. This

recommendation reflects the possibility of undiagnosed HIV infection, which would significantly alter the risk-benefit balance of short-course antiretroviral therapy. It may be possible for service providers to obtain results more rapidly by considering newer technologies, such as saliva testing or rapid serum HIV testing. However, such testing should follow the conventional norms of informed consent.

Those presenting for PEPSE must be seen in a GU Medicine/HIV department at the earliest opportunity. It is recommended that the individual be referred to a Health Adviser (or appropriately experienced health care worker), where the following issues can be addressed:

- Pre-test discussion (if HIV status as yet unknown)
- The need to continue with a further four-week course of PEPSE if the baseline result is negative
- The need to have a follow-up HIV test at three and six months
- The side effects of the drugs and the support available in the clinic and in the community to help adherence
- The need to utilize generic social support over the following three to six months
- The need for safer sex for the following six months
- Issues around disclosure
- Coping strategies
- For patients concerned about sexual risk taking health advisers can offer ongoing risk reduction work or referral to psychology if appropriate

Follow-Up Arrangements for Individuals Presenting for PEPSE

Regular medical follow-up is necessary for individuals receiving PEPSE to monitor tolerability and possible toxicity of the medications. Close follow-up and encouragement, ideally on a weekly basis at first, is likely to improve adherence to the treatment regimen and allow prompt management of any concerns or complications.

It is recommended that all individuals who receive PEPSE (and those who decline but have had significant risk of exposure to HIV) be re-tested for HIV antibodies at three and six months.

At present there is no prospective monitoring scheme for individuals receiving PEPSE, but it is anticipated this may be developed in conjunction with the Health Protection Agency.

Any adverse events attributed to antiretroviral medications should be reported via the HIV Adverse Drug Reactions Reporting Scheme.

Additional Management of Individuals after Potential Sexual Exposure to HIV

It is recommended that all individuals presenting for PEPSE be comprehensively screened for other STIs at an appropriate time point, in accordance with the guidelines on screening for STIs (accessible at [www.bashh.org]). It is essential that Hepatitis B vaccination (and immunoglobulin) be considered in addition to

PEP in accordance with existing guidance. Additionally, the opportunity should be taken for appropriate risk-reduction discussion with individuals presenting for PEPSE.

Other Issues Relating to Sexual Exposure to HIV

Dissemination of Information Regarding PEPSE to Individuals Who May Be At Risk of HIV Transmission

It is recommended that information regarding PEPSE should be proactively provided to individuals diagnosed with HIV infection, particularly if in a serodiscordant relationship. Furthermore, uninfected individuals with potential for future exposure to HIV, should be provided with information regarding PEPSE in addition to full discussion of other proven risk-reduction strategies. It is recognized that community-based organizations will have a large part to play in providing this information. Consideration should be given to provision of 24-hour helpline access to enable individuals to establish whether presentation to hospital services for PEPSE is appropriate.

Management of Individuals Who Repeatedly Present for PEPSE or with Ongoing Risk Behaviour

There is also a concern regarding repeat users of PEPSE. However, once again, there is no data suggesting that a significant number of individuals will utilize PEPSE repeatedly, perhaps due to the aversive nature of the medications. It is therefore recommended that individuals be considered for repeat courses of PEPSE according to the risk of HIV acquisition at the time of presentation, particularly if their circumstances suggest this to be appropriate (commercial sex workers, serodiscordant couples, inability to control the preventative behaviour of their partners). However, it is also recommended that repeat attenders be strongly encouraged to discuss these issues with a Health Advisor and/or Psychologist.

Individuals who present more than once a year for PEPSE, who do not otherwise have prevailing circumstances for doing so, are of greater concern and should be referred at an early stage for discussions around their safer sex strategies. They should still be considered for PEPSE if the current risk circumstances clearly indicate a need for this, but that this is conditional on their attendance for discussions around future safer sex strategies.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated for each recommendation. In general, the recommendations are based upon a

combination of biological plausibility, cohort studies, data from post-exposure prophylaxis (PEP) in other settings, and expert opinion.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Reduced transmission of human immunodeficiency virus (HIV) following sexual exposure to HIV

POTENTIAL HARMS

Side Effects of Antiretroviral Drugs

Any of the antiretroviral drugs may have side effects, which appear to be less well tolerated in human immunodeficiency virus (HIV)-negative patients receiving post-exposure prophylaxis than HIV-positive individuals starting treatment.

Specific Side Effects of Protease Inhibitors

- Metabolic abnormalities
- Lipid abnormalities
- Insulin Resistance
- Diabetes mellitus
- Gastro-intestinal side effects

Other

Poor adherence of PEP regimens theoretically may result in the acquisition of a drug-resistant virus, should the individual become HIV-infected. This has been suggested as a risk for subsequent seroconversion in a retrospective analysis of post-exposure prophylaxis following potential sexual exposure (PEPSE) failures.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgment of the clinician and consideration of individual patient circumstances and wishes. It should be acknowledged that use of any antiretroviral agent in this setting is an unlicensed indication. All possible care has been undertaken to ensure the publication of the correct dosage and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The provision of post-exposure prophylaxis (PEP) following sexual exposure requires consideration of appropriate pathways of care between genitourinary medicine/human immunodeficiency virus (HIV) clinicians and those providing access to emergency and primary care in order to ensure post-exposure prophylaxis following potential sexual exposure (PEPSE) is administered both appropriately and in a timely fashion. This will require local interpretation of this guideline and will most likely involve a degree of organizational change and provision of additional resources.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Chart Documentation/Checklists/Forms

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Fisher M, Benn P, Evans B, Pozniak A, Jones M, Maclean S, Davidson O, Summerside J, Hawkins D, Clinical Effectiveness Group (British Association for Sexual Health and HIV). UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure. Int J STD AIDS 2006 Feb;17(2):81-92. [84 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Feb

GUIDELINE DEVELOPER(S)

British Association for Sexual Health and HIV - Medical Specialty Society

SOURCE(S) OF FUNDING

No specific or external funding was sought or provided in the development of this guideline.

GUIDELINE COMMITTEE

Clinical Effectiveness Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Clinical Effectiveness Group (CEG) Members: Keith Radcliffe (*Chairman*), Imytaz Ahmed-Jushuf; Mark Fitzgerald; Guy Rooney; Jan Welch

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [British Association for Sexual Health and HIV Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

Auditable outcome measures and example of potential sexual exposure (PEPSE) proforma are provided in the [original guideline document](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on June 9, 2008. The information was verified by the guideline developer on August 13, 2008.

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